

Amendment to the Claims

A listing of the claims presented in this patent application appears below. The listing replaces all prior versions and listings of the claims in this patent application.

1. (Original) A method for identifying a mammalian glioma tumor that is likely to respond, or is responsive to an EGFR polypeptide (SEQ ID NO: 7) inhibitor or an mTOR polypeptide (SEQ ID NO: 2) inhibitor, the method comprising examining a sample obtained from the tumor for:

(a) the expression of PTEN polypeptide (SEQ ID NO: 5);

and the presence of at least one of,

(b) phosphorylated S6 ribosomal polypeptide (SEQ ID NO: 1);

(c) EGFR polypeptide (SEQ ID NO: 7)

(d) phosphorylated AKT polypeptide (SEQ ID NO: 4); and

(e) phosphorylated ERK polypeptide (SEQ ID NO: 8)

wherein decreased expression of PTEN polypeptide together with decreased phosphorylation of S6 ribosomal polypeptide in the sample, as compared to a control, identifies the glioma tumor as likely to respond or responsive to an mTOR inhibitor, and

wherein decreased expression an of PTEN together with normal phosphorylation of S6 ribosomal polypeptide in the sample, as compared to a control, identifies the glioma tumor as not likely to respond or unresponsive to an mTOR inhibitor, and

wherein normal or increased expression of PTEN and increased expression and/or activity of EGFR together with increased phosphorylation of AKT and/or phosphorylation of ERK identifies the glioma tumor as not likely to respond and/or unresponsive to an EGFR inhibitor.

2. (Original) The method of claim 1, wherein the phosphorylation of S6 ribosomal polypeptide is determined subsequent to contacting the tumor or sample with an mTOR inhibitor.

3. (Original) The method of claim 1, wherein the phosphorylation of AKT and/or ERK is determined subsequent to contacting the tumor or sample with an EGFR inhibitor.

4. (Original) The method of claim 1, wherein the mTOR inhibitor is rapamycin, SDZ-RAD, CCI-779, RAD 001, or AP23573.

5. (Original) The method of claim 1, wherein the EGFR inhibitor is ZD-1839, OSI-774, PD-153053, PD-168393, IMC-C225 or CI-1033.
6. (Currently amended) The method of claim 1, wherein the expression of (a) and one or more of (ab)-(e) is examined using an antibody.
7. (Original) The method of claim 6, wherein the presence of phosphorylated S6 ribosomal polypeptide (SEQ ID NO: 1) is examined using an antibody that binds an epitope comprising a phosphorylated serine residue at position 235 in SEQ ID NO: 1.
8. (Original) The method of claim 6, wherein the presence of EGFR and PTEN are examined using an EGFR-specific antibody and PTEN-specific antibody, respectively.
9. (Original) The method of claim 6, wherein the presence of phosphorylated AKT (SEQ ID NO: 4) is examined using an antibody that binds an epitope comprising a phosphorylated serine residue at position 473 in SEQ ID NO: 4.
10. (Original) The method of claim 6, wherein the presence of phosphorylated ERK is examined using an antibody that binds an epitope comprising a phosphorylated threonine residue at position 202 or a phosphorylated tyrosine residue at position 204 in SEQ ID NO: 8.
11. (Original) The method of claim 1, wherein the glioma tumor is a glioblastoma multiforme tumor.
12. (Original) The method of claim 1, wherein the sample is a paraffin embedded biopsy sample.
13. (Original) A method for identifying a mammalian glioma tumor that does not express a PTEN polypeptide (SEQ ID NO: 5) and which is likely to respond or is responsive to an inhibitor of mTOR polypeptide (SEQ ID NO: 2) activity, the method comprising examining a sample obtained from the tumor for the presence of phosphorylated S6 ribosomal polypeptide (SEQ ID NO: 1) after contacting the tumor or the sample with the inhibitor,

wherein, an observable decrease in phosphorylated S6 ribosomal polypeptide in the sample, as compared to a control that is not contacted with the inhibitor identifies the glioma tumor as likely to respond or responsive to the inhibitor, and

wherein no observable decrease in phosphorylated S6 ribosomal polypeptide in the sample, as compared to a control identifies the glioma tumor as not likely to respond or unresponsive to the inhibitor.

14. (Original) The method of claim 13, wherein the glioma tumor is glioblastoma multiforme.

15. (Currently amended) The method of claim 13, wherein the glioma is identified as a tumor that does not express a PTEN polypeptide (SEQ ID NO: 5) using an antibody that binds the PTEN polypeptide (SEQ ID NO: 5).

16. (Withdrawn) A method for identifying a mammalian glioma tumor that expresses a PTEN polypeptide (SEQ ID NO: 5) and which is not likely to respond or is nonresponsive to an inhibitor of EGFR polypeptide (SEQ ID NO: 7) activity, the method comprising examining a sample obtained from the tumor for the presence of EGFR (SEQ ID NO: 7) and the presence of a phosphorylated AKT polypeptide (SEQ ID NO: 4) or the presence of a phosphorylated ERK polypeptide (SEQ ID NO: 8), after contacting the tumor or the sample with the inhibitor,

wherein an increase in the levels of the EGFR polypeptide and the levels of phosphorylated AKT polypeptide or phosphorylated ERK polypeptide identifies the glioma tumor as not likely to respond or nonresponsive to the inhibitor.

17. (Withdrawn) The method of claim 16, wherein the a sample obtained from the tumor is examined for the presence of a phosphorylated AKT polypeptide (SEQ ID NO: 4) and the presence of a phosphorylated ERK polypeptide (SEQ ID NO: 8).

18. (Withdrawn) The method of claim 16, wherein the glioma tumor is glioblastoma multiforme.

19. (Withdrawn) The method of claim 16, wherein the glioma is identified a tumor that expresses a PTEN polypeptide (SEQ ID NO: 5) using an antibody that binds the PTEN polypeptide (SEQ ID NO: 5).

20. (Currently Amended) A kit for characterizing a mammalian glioma tumor or cell, the kit comprising:

(a) an antibody that binds PTEN (SEQ ID NO: 5);

and one or more of the following:

(b) an antibody that binds phosphorylated S6 ribosomal polypeptide (SEQ ID NO: 1);

- (c) an antibody that binds EPGGFR (SEQ ID NO: 7);
 - (d) an antibody that binds phosphorylated AKT (SEQ ID NO: 4); and
 - (e) an antibody that binds phosphorylated ERK (SEQ ID NO: 8).
21. (Original) The kit of claim 20, wherein the kit comprises a plurality of antibodies selected from the group consisting of (b)-(e).
22. (Original) The kit of claim 20, wherein:
- the antibody of (b) is specific for S6 ribosomal polypeptide (SEQ ID NO: 1) having a phosphorylated serine residue at position 235 in SEQ ID NO: 1;
 - the antibody of (d) is specific for AKT (SEQ ID NO: 4) having a phosphorylated serine residue at position 473 in SEQ ID NO: 4; and
 - the antibody of (e) is specific for ERK having a phosphorylated threonine residue at position 202 and tyrosine 204 in SEQ ID NO: 8.
23. (Original) The kit of claim 20, wherein the kit further includes an antibody that binds Ki-67 polypeptide (SEQ ID NO: 9), p-H3 histone polypeptide (SEQ ID NO: 10) or caspase-3 polypeptide (SEQ ID NO: 11).
24. (Original) The kit of claim 20, wherein the kit further includes; and at least one secondary antibody that binds to an antibody (a)-(e).